

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 - 35. (Cancelled)

36. (Currently amended) A non-human transgenic mammal, [which comprises] comprising an endogenous IgH locus which is modified by [replacing] replacement of a switch sequence S_μ with [all or a part of] a transgene comprising ~~consisting of a C_α gene for a human class A immunoglobulin heavy chain constant region gene C_α or a segment of said C_α gene~~, comprising at least an exon encoding the CH3 domain and a membrane exon.

37. (Previously presented) The non-human transgenic mammal of claim 36, which is homozygous for said modified IgH locus.

38. (Currently amended) The non-human transgenic mammal of claim 36, wherein said endogenous IgH locus is modified by replacement of the switch sequence S_μ, with the entire C_α gene.

39. (Currently amended) The non-human transgenic mammal of claim 36, wherein said endogenous IgH locus is modified by replacement of the switch sequence S_μ with the segment of the C_α gene comprising the exon encoding the CH3 domain and the membrane exon.

40. (Currently amended) The non-human transgenic mammal of claim 36, wherein said C_α gene is the C_{α1} gene.

41. (Previously presented) The non-human transgenic mammal of claim 36, which further comprises another transgene encoding a human immunoglobulin light chain.

42. (Currently amended) The non-human transgenic mammal of claim 41, wherein said light chain is a kappa light chain.

43. (Currently amended) The non-human transgenic mammal of claim 41~~2~~, wherein said ztransgene which encodes a human immunoglobulin kappa light chain, further comprises the intronic activator E μ upstream of a DNA sequence encoding said human immunoglobulin kappa light chain and the palindrome *hs3a/hs1,2/hs3b* downstream of said DNA sequence.

44. (Previously presented) The non-human transgenic mammal of claim 43, wherein said transgene is under the control of the promoter of the human immunoglobulin heavy chain.

45. (Previously presented) The non-human transgenic mammal of claim 41, which is dizygous for said transgene.

46. (Currently amended) The non-human transgenic mammal of claim 41, further comprising~~which possesses an~~ inactivated endogenous immunoglobulin kappa light chain locus ~~of the inactivated kappa chain~~.

47. (Currently amended) The non-human transgenic mammal of claim 46, which is homozygous for said inactivated endogenous immunoglobulin kappa light chain locus ~~of the inactivated kappa gene~~.

48. (Currently amended) The non-human transgenic mammal of claim 36, further comprising ~~which possesses a gene encoding the~~ an inactivated endogenous J chain gene.

49. (Currently amended) The non-human transgenic mammal of claim 48, which is homozygous for said inactivated endogenous J chain gene ~~encoding the inactivated J chain gene~~.

50. (Currently amended) The non-human transgenic mammal of claim 48, which further comprises another transgene encoding a human immunoglobulin J chain gene.

51. (Previously presented) The non-human transgenic mammal of claim 36, which is a transgenic mouse.

52. (Currently amended) A transgenic mouse of claim 51, which comprises:

a) an endogenous IgH locus modified by replacement of the switch sequence S μ with the entire ~~C α 1 gene for a human class A immunoglobulin~~ heavy chain constant region gene C α 1, and

b) a human kappa light chain transgene ~~complete V κ gene~~ comprising ~~rearranged a~~ V κ I gene rearranged with a J κ 5 gene, ~~the a~~ J κ -C κ intron and a C κ gene, under the transcriptional control of ~~the promoter~~ of the human heavy chain promoter (pVH), the intronic activator E μ upstream of said promoter and the palindrome *hs3a/hs1,2/hs3b* downstream of said C κ gene.

53. (Currently amended) A homologous recombination targeting vector, which comprises a human class A immunoglobulin heavy chain constant region gene ~~C α gene for a human class A immunoglobulin~~ or a segment of the said C α gene comprising at least an exon encoding the a CH3 domain and a membrane exon, flanked by fragments of sequences of the IgH locus from a non-human mammal which are adjacent to a switch sequence S μ ~~sequence~~.

54. (Previously presented) The targeting vector of claim 53, which comprises a cassette for expressing a selection marker, adjacent to said C α gene or to a segment of said gene.

55. (Previously presented) The targeting vector of claim 54, wherein said expression cassette is flanked by site-specific recombination sequences.

56. (Currently amended) The targeting vector of claim 55[4], wherein said sequences are LoxP sequences of Cre recombinase.

57. (Currently amended) The targeting vector of claim 53, wherein said fragments of sequences of the IgH locus which are adjacent to the switch sequence S μ ~~sequence~~ are fragments of the mouse IgH locus ~~of murine origin~~.

58. ((Currently amended) The targeting vector of claim 57[6], wherein ~~the C α gene or the segment of said gene is flanked, in 5' and in 3' respectively, by~~ said fragments consist[ing] of the sequences SEQ ID NO: 7 and SEQ ID NO: 8, corresponding respectively to positions 131281 to 136441 and 140101 to 145032 in the sequence of murine chromo[some] 12 (accession number AC073553 in the EMBL/GenBank database).

59. (Previously presented) An embryonic cell of a nonhuman mammal, modified with the targeting vector of claim 53.

60-73 (Withdrawn)